REMARKS

Applicants have studied the Office Action mailed June 4, 2003 and have made amendments to the claims. It is respectfully submitted that the application, as amended, is in condition for allowance. Reconsideration and allowance of the pending claims in view of the above amendments and the following remarks is respectfully requested.

Rejection of claims 4, 8-9, and 24-29 under 35 USC §101, utility, and §112, 1st paragraph:

The Examiner has rejected claims 4, 8-9, and 24-29 under 35 U.S.C.§101 and §112, 1st paragraph. In summary, the Examiner has stated that the claimed invention is not supported by either a specific, substantial, credible asserted utility or a well-established utility, and, consequently, one skilled in the art would not know how to use the claimed invention.

The Examiner states that the instant claims are drawn to a protein of as yet undetermined function or biological significance. The Examiner asserts that there is no evidence of record or any line of reasoning that would support a conclusion that the ras-like protein of the instant application was, as of the filing date, useful for the diagnosis, prevention and treatment of inflammation and disorders associated with proliferation and apoptosis. The Examiner continues by stating that until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO:2, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Thus, the Examiner states that, since the instant specification does not disclose a credible "real world" use for the ras-like protein of the instant invention, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

Applicants respectfully traverse this rejection based on the following remarks.

Contrary to the Examiner's assertions, the claimed isolated nucleic acid molecules, such as SEQ ID NOS:1 and 3, that encode a specified amino acid sequence, SEQ ID NO:2, and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 U.S.C.§101 and the first paragraph of 35 U.S.C.§112. These, as well as the accepted state of the art view that such molecules have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets, establishes the utility of the claimed invention.

The utility requirement of a claimed invention requires that an invention must have a specific, substantial and credible utility. These requirements are defined in broad terms in cases such as *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) and the recently adopted Utility Guidelines from the USPTO.

However, the notion that a recognized valuable addition to even entry points of the drug discovery cycle advances the art sufficient to establish a "usefulness" of a claimed invention should not be ignored. This is supported by previous case law (e.g., *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980)). Accordingly, the present invention, which is drawn to isolated nucleic acid molecules that encode a novel ras-like protein (SEQ ID NO:2), has valuable commercial utilities in the drug discovery process by providing previously unidentified members of an important pharmaceutical target class. The present invention provides sufficient knowledge and information that is beneficial to the public, and provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. It is well recognized that ras-like proteins are among the most important target for drug action (see, e.g., pages 1-5 of the specification). The public disclosure of a new member of the ras-like family through the patenting process clearly advances the art and augments the capabilities of biomedical researchers to combat illnesses.

The utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). *Juicy Whip* held that, in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful result." The polypeptides and encoding nucleic acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc. Therefore, the present invention is not "totally incapable of achieving a useful result." Instead, it is useful.

Contrary to the Examiner's assertions, Applicants have provided sufficient guidance such that undue experimentation would not be required for one of ordinary skill in the art to comprehend the function and biological significance of the disclosed polypeptides and encoding polynucleotides so as to be able to use the claimed invention. For example, the function of RhoGAP proteins, such as Nadrin, is well established in the art and specifically asserted in the specification. For example, Rho proteins are one of five subfamilies within the Ras superfamily

(as indicated on lines 11-12 of page 3 of the specification), and Rho proteins are important for controlling signal transduction in the process of linking receptors of growth factors to actin polymerization which is necessary for cell division (as indicated on lines 13-15 of page 3). Furthermore, during cell adhesion, Rho proteins are essential for triggering focal complex assembly and integrin-dependent signal transduction (as indicated on lines 25-27 of page 4). GTPase-activating proteins (including RhoGAP proteins) inactivate Ras proteins (including Rho proteins), which alternate between an inactive form bound to GDP and an active form bound to GTP (as indicated on lines 7-10 of page 2). Thus, because it is well established in the art that RhoGAP proteins are important for inactivating Rho proteins, which are in turn important for regulating signal transduction, cell adhesion, and cell division, it is well established that novel RhoGAP proteins are useful in the treatment, diagnosis, and prevention of cancer. Such functions are quite specific for the family of ras-like proteins and differentiate them from other proteins. As such, these functions are specific enough to define a use for novel ras-like proteins and encoding nucleic acid molecules in the drug discovery process and to enable one of ordinary skill in the art to use the claimed invention without undue experimentation.

Because of the essential roles that ras-like proteins play in regulating signal transduction, cell adhesion, and cell division, it is clear that the disclosure of novel ras-like proteins satisfies a need in the art by providing important new compositions that are useful towards the prevention, diagnosis, and treatment of cancer. Consequently, one of ordinary skill in the art would recognize that novel ras-like proteins, and encoding nucleic acid molecules, have "real world" uses that meet the requirements of 35 U.S.C.§101.

Thus, there is overwhelming evidence in the art to support the utility of novel ras-like proteins and encoding nucleic acid molecules. Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the ras-like family of proteins, and each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

By placing a new member of the ras-like protein family into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further discovery. The Utility requirement cannot be used to contradict the reasons for the patent system,

i.e., to encourage early disclosures of inventions so that others can benefit from, improve upon, and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new ras-like proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

The grant of a patent to the claimed isolated nucleic acid molecule and the resultant disclosure of the nucleic acid and protein sequences to the public will certainly shorten the process for medical researchers to discover other novel uses for the present nucleic acid molecules which encode ras-like proteins. One example disclosed in the specification is that the present nucleic acid molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents that bind to a protein target and modulate cellular processes such as signal transduction can subsequently be developed and refined for use in mammalian therapeutic applications. All of this later discovery and refinement will be done using the presently claimed material. These uses are clearly commercial and substantial uses that are specific for a very limited number of proteins/nucleic acid molecules.

In addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112. The claimed invention is directed to nucleic acid sequences, such as SEQ ID NOS:1 and 3, that encode a ras-like protein with a specified amino acid sequence (SEQ ID NO:2). Exemplary uses of the nucleic acid sequences are clearly recited in the specification on, for example, pages 35-54. Among the examples, the nucleic acid molecules are useful as hybridization probes for messenger RNA molecules, transcript/cDNA molecules, genomic DNA, and variants thereof. An expression vector comprising the nucleic acid sequences can be constructed that expresses the ras-like protein. Such uses are specific for the claimed nucleic acid molecules, and the products of such uses will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different nucleic acid molecule for the same purpose.

In view of law and fact, the utility standard interpreted by the USPTO guidelines is too high. The commercial value of previously unidentified members of the ras-like protein family, members of which are well known in the art to be commercially valuable drug targets, should be

sufficient to satisfy the utility requirement. Therefore, applicants respectfully request that the Examiner withdraw the rejections.

Rejection of claims 8, 9, and 27-29 under 35 USC §101, statutory subject matter, and §112, 1st paragraph:

The Examiner has rejected claims 8-9, and 27-29 under 35 U.S.C.§101 as being directed to non-statutory subject matter since the claims can be interpreted as being drawn to a vector or host cell within a human. Moreover, the Examiner also rejected claims 8-9, and 27-29 under 35 U.S.C. §112, 1st paragraph, asserting that the specification, while being enabling for an isolated expression vector and host cell in vitro, does not reasonably provide enablement for an isolated expression vector or host cell in vivo.

Applicants have hereby amended claims 8 and 9, as indicated above, to clarify that the claims are directed to isolated in vitro vectors and host cells, respectively.

Conclusions

Claims 8 and 9 have been amended by the present response. As such, claims 4, 8-9, 13, and 24-29 remain pending, and claim 13 remains withdrawn from consideration.

The amendments to the claims add no new subject matter and their entry is respectfully requested.

In view of the above remarks and amendments, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent at (240) 453-3812 should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,

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Date: October 6, 2003

By: _____

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